AMENDMENTS TO THE SPECIFICATION

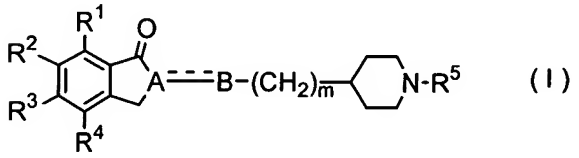
IN THE SPECIFICATION:

Page 6

Please amend the paragraph beginning on page 6 line 8 through page 17 line 1 as follows:

Specifically, the present invention relates to:

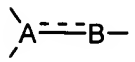
1) a sigma receptor binding agent comprising an indanone compound represented by the formula:



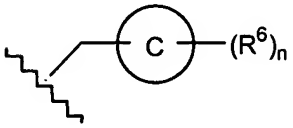
(I)

(in the formula (I), R^1, R^2, R^3 and R^4 are the same as or different from each other and each represents hydrogen atom, a halogen atom, hydroxyl group, nitrile group, a C_{1-6} alkyl group which may be substituted, a cycloalkyl group having three to eight carbon atoms which may be substituted, a C_{1-6} alkoxy group which may be substituted, a cycloalkoxy group having three to eight carbon atoms which may be substituted, a C_{1-6} acyl group which may be substituted, a C_{1-6} alkoxycarbonyl group having which may be substituted, a C_{1-6} alkylaminocarbonyloxy group which may be substituted, a di(C_{1-6} alkyl)aminocarbonyloxy group which may be substituted, nitro group, an amino group which may be substituted, an amide group which may be substituted, mercapto group or a thio-C_{1-6} alkoxy group which may be substituted, and further R^1 with R^2, R^2 with R^3, or R^3 with R^4 may together form an aliphatic ring, an

aromatic ring, a heterocyclic ring or an alkylenedioxy ring; the partial structure:



represents a group represented by >CH-CH_2-, >C=CH- or >C(-R^7)-CH_2-; m represents an integer of 0 or 1 to 5; and R^5 represents hydrogen atom, a C_{1-6} alkyl group which may be substituted, a C_{2-6} alkenyl group which may be substituted, a C_{2-6} alkynyl group which may be substituted, a cycloalkyl group having three to eight carbon atoms which may be substituted, a 2,2-(alkylenedioxy)ethyl group or a group represented by the formula:



(wherein the ring C represents benzene ring, an aliphatic ring or a heterocyclic ring; R^6s are the same as or different from each other and each represents hydrogen atom, a halogen atom, hydroxyl group, nitrile group, a C_{1-6} alkyl group which may be substituted, a C_{2-6} alkenyl group which may be substituted, a C_{2-6} alkynyl group which may be substituted, a cycloalkyl group having three to eight carbon atoms which may be substituted, a C_{1-6} alkoxy group which may be substituted, a C_{1-6} alkoxyalkoxy group which may be substituted, an aryloxy group which may be substituted or an aralkyloxy group which may be substituted, and further two of R^6s may together form an aliphatic ring, an aromatic ring, a heterocyclic ring or an alkylenedioxy ring; R^7 represents a halogen atom, hydroxyl group, a C_{1-6} alkyl group, a C_{1-6} alkoxy

group, nitrile group, a halogeno-C_{1-6} alkyl group, a hydroxyl-C_{1-6} alkyl group, a cyano-C_{1-6} alkyl group, an amino-C_{1-6} alkyl group, nitro group, azide group, an amino group which may be substituted, carbamoyl group which may be substituted, carboxyl group which may be substituted, mercapto group or a thio-C_{1-6} alkoxy group; and n represents an integer of 1 to 5), provided that 1-benzyl-4-[(5,6-dimethoxy-1-indanon)-2-yl]methylpiperidine, a pharmacologically acceptable salt thereof or a hydrate of them are excluded), a pharmacologically acceptable salt thereof or a hydrate of them; 2) the sigma receptor binding agent comprising an indanone compound, a pharmacologically acceptable salt thereof or a hydrate of them described in 1), wherein the indanone compound represented by the formula (I) is one selected from:

(1) 1-benzyl-4-[(5,6-dimethoxy-1-indanon)-2-ylidene]methylpiperidine,

(2) 1-benzyl-4-[(5,6-diethoxy-1-indanon)-2-ylidene]methylpiperidine,

(3) 1-benzyl-4-[(1-indanon)-2-yl]methylpiperidine,

(4) 1-benzyl-4-[(5-methoxy-1-indanon)-2-yl]methylpiperidine,

(5) 1-benzyl-4-[(5-ethoxy-6-methoxy-1-indanon)-2-yl]methylpiperidine,

(6) 1-benzyl-4-[(5,6-diethoxy-1-indanon)-2-yl]methylpiperidine,

(7) 1-benzyl-4-[[5,6-di(1-propyloxy)-1-indanon)-2-yl]methylpiperidine,

(8) 1-benzyl-4-[2-[(5,6-dimethoxy-1-indanon)-2-yl]ethyl]piperidine,

(9) 1-benzyl-4-[3-[(5,6-dimethoxy-1-indanon)-2-yl]propyl]piperidine,

(10) 1-(3-fluorobenzyl)-4-[(5,6-dimethoxy-1-indanon)-2-yl]methylpiperidine,

(11) 1-(3-methylbenzyl)-4-[(5,6-dimethoxy-1-indanon)-2-yl]methylpiperidine,

(12) 1-cyclohexylmethyl-4-[(5,6-dimethoxy-1-indanon)-2-yl]methylpiperidine,

(13) 1-benzyl-4-[(2-fluoro-1-indanon)-2-yl]methylpiperidine,

(14) 1-benzyl-4-[(5-methoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine,

(15) 1-benzyl-4-[(5,6-dimethoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine,

(16) 1-benzyl-4-[(5,6-diethoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine,

(17) 1-benzyl-4-[[5,6-di(1-propyloxy)-2-fluoro-1-indanon]-2-yl]methylpiperidine,

(18) 1-benzyl-4-[(5,6-dimethoxy-2-fluoro-1-indanon)-2-yl]piperidine,

(19) 1-benzyl-4-[2-[(5,6-dimethoxy-2-fluoro-1-indanon)-2-yl]ethyl]piperidine,

(20) 1-benzyl-4-[3-[(5,6-dimethoxy-2-fluoro-1-indanon)-2-yl]propyl]piperidine,

(21) 1-(2-fluorobenzyl)-4-[(5,6-dimethoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine,

(22) 1-(3-fluorobenzyl)-4-[(5,6-dimethoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine,

(23) 1-(4-fluorobenzyl)-4-[(5,6-dimethoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine,

(24) 1-(3-methylbenzyl)-4-[(5,6-dimethoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine,

(25) 1-cyclohexylmethyl-4-[(5,6-dimethoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine,

(26) 1-benzyl-4-[(5,6-dimethoxy-2-chloro-1-indanon)-2-yl]methylpiperidine,

(27) 1-benzyl-4-[(5,6-diethoxy-2-chloro-1-indanon)-2-yl]methylpiperidine,

(28) 1-benzyl-4-[(5-ethoxy-6-methoxy-2-chloro-1-indanon)-2-yl]methylpiperidine,

(29) 1-benzyl-4-[(5,6-dimethoxy-2-bromo-1-indanon)-2-yl]methylpiperidine, and

(30) 1-benzyl-4-[(5,6-dimethoxy-2-methyl-1-indanon)-2-yl]methylpiperidine; 3) the sigma receptor binding agent described in 1) or 2), which is a sigma receptor antagonist or a sigma receptor agonist; 4) the sigma receptor binding agent described in 1) or 2), which is an agent for preventing, treating or improving a disease against which a sigma receptor agonistic drug is efficacious; 5) the sigma receptor binding agent described in 1) or 2), which is an agent for preventing, treating or improving a disease against which a sigma receptor antagonistic action is efficacious; 6) the sigma receptor binding agent described in 1) or 2), which is an agent for preventing, treating or improving a disease against which a sigma receptor agonistic action is efficacious; 7) the sigma receptor binding agent described in

1) or 2), which is an agent for preventing, treating or improving a mental disorder; 8) the sigma receptor binding agent described in 7), wherein the mental disorder is at least one selected from a disorder accompanied with cerebrovascular dementia and/or senile dementia, schizophrenia, emotional disorder, depression, neurosis, psychophysiologic disorder and anxiety; 9) the sigma receptor binding agent described in 8), wherein the disorder accompanied with cerebrovascular dementia and/or senile dementia is at least one selected from aggressive behavior, mental excitement, wandering, delirium, hallucination and hyperkinesis; 10) the sigma receptor binding agent according to claim 1 or 2, which is an agent for improving intellectual function; 11) the indanone compound, a pharmacologically acceptable salt thereof or a hydrate of them, wherein the indanone compound represented by the formula (I) is one selected from:

(1) 1-benzyl-4-[[5,6-(1,2-ethylenedioxy)-1-indanon]-2-ylidene]methylpiperidine,

(2) 1-benzyl-4-[(5-cyclohexyl-1-indanon)-2-ylidene]methylpiperidine,

(3) 1-benzyl-4-[(5-cyclohexyloxy-6-methoxy-1-indanon)-2-ylidene]methylpiperidine,

(4) 1-benzyl-4-[[5-methoxy-6-(2-propyloxy)-1-indanon]-2-ylidene]methylpiperidine,

(5) 1-benzyl-4-[[5,6-(1,2-ethylenedioxy)-1-indanon]-2-yl]methylpiperidine,

(6) 1-benzyl-4-[[5,6-cyclohexyl-1-indanon]-2-yl]methylpiperidine,

(7) 1-benzyl-4-[(5-cyclohexyloxy-6-methoxy-1-indanon)-2-yl]methylpiperidine,

(8) 1-benzyl-4-[[5-methoxy-6-(2-propyloxy)-1-indanon]-2-yl]methylpiperidine,

(9) 1-benzyl-4-[(6-ethoxy-5-methoxy-1-indanon)-2-yl]methylpiperidine,

(10) 1-benzyl-4-[[6-methoxy-5-(1-propyloxy)-1-indanon]-2-yl]methylpiperidine,

(11) 1-benzyl-4-[(5-cyanomethoxy-6-methoxy-1-indanon)-2-yl]methylpiperidine,

(12) 1-cyclopentylmethyl-4-[(5,6-diethoxy-1-indanon)-2-yl]methylpiperidine,

(13) 1-cyclohexylmethyl-4-[(5,6-diethoxy-1-indanon)-2-yl]methylpiperidine,

(14) 1-cycloheptylmethyl-4-[(5,6-diethoxy-1-indanon)-2-yl]methylpiperidine,

(15) 1-cyclooctylmethyl-4-[(5,6-diethoxy-1-indanon)-2-yl]methylpiperidine,

(16) 1-(2-fluorobenzyl)-4-[(5,6-diethoxy-1-indanon)-2-yl]methylpiperidine,

(17) 1-(3-fluorobenzyl)-4-[(5,6-diethoxy-1-indanon)-2-yl]methylpiperidine,

(18) 1-(4-fluorobenzyl)-4-[(5,6-diethoxy-1-indanon)-2-yl]methylpiperidine,

(19) 1-(2-chlorobenzyl)-4-[(5,6-diethoxy-1-indanon)-2-yl]methylpiperidine,

(20) 1-(3-chlorobenzyl)-4-[(5,6-diethoxy-1-indanon)-2-yl]methylpiperidine,

(21) 1-(4-chlorobenzyl)-4-[(5,6-diethoxy-1-indanon)-2-yl]methylpiperidine,

(22) 1-(2-methylbenzyl)-4-[(5,6-diethoxy-1-indanon)-2-yl]methylpiperidine,

(23) 1-(3-methylbenzyl)-4-[(5,6-diethoxy-1-indanon)-2-yl]methylpiperidine,

(24) 1-(4-methylbenzyl)-4-[(5,6-diethoxy-1-indanon)-2-yl]methylpiperidine,

(25) 1-benzyl-4-[(6-ethoxy-5-methoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine,

(26) 1-benzyl-4-[(5-ethoxy-6-methoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine,

(27) 1-benzyl-4-[[6-methoxy-5-(1-propyloxy)-2-fluoro-1-indanon]-2-yl]methylpiperidine,

(28) 1-(2-fluorobenzyl)-4-[(5,6-diethoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine,

(29) 1-(3-fluorobenzyl)-4-[(5,6-diethoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine,

(30) 1-(4-fluorobenzyl)-4-[(5,6-diethoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine,

(31) 1-(2-chlorobenzyl)-4-[(5,6-diethoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine,

(32) 1-(3-chlorobenzyl)-4-[(5,6-diethoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine,

(33) 1-(4-chlorobenzyl)-4-[(5,6-diethoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine,

(34) 1-(2-methylbenzyl)-4-[(5,6-diethoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine,

(35) 1-(3-methylbenzyl)-4-[(5,6-diethoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine,

(36) 1-(4-methylbenzyl)-4-[(5,6-diethoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine,

(37) 1-cyclopentylmethyl-4-[(5,6-diethoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine,

(38) 1-cyclohexylmethyl-4-[(5,6-diethoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine,

(39) 1-cycloheptylmethyl-4-[(5,6-diethoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine,

(40) 1-cyclooctylmethyl-4-[(5,6-diethoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine,

(41) 1-benzyl-4-[(5-cyanomethoxy-6-methoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine,

(42) 1-(3,4-difluorobenzyl)-4-[(5,6-diethoxy-1-indanon)-2-yl]methylpiperidine,

(43) 1-(3,5-difluorobenzyl)-4-[(5,6-diethoxy-1-indanon)-2-yl]methylpiperidine,

(44) 1-(3,4-difluorobenzyl)-4-[(5,6-diethoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine, and

(45) 1-(3,5-difluorobenzyl)-4-[(5,6-diethoxy-2-fluoro-1-indanon)-2-yl]methylpiperidine; 12) a pharmaceutical composition comprising the indanone compound described in 11), a

pharmacologically acceptable salt thereof or a hydrate of them; 13) the pharmaceutical composition according to claim 12, which is a sigma receptor binding agent; 14) the pharmaceutical composition described in 12), which is a sigma receptor antagonist or a sigma receptor agonist; 15) the pharmaceutical composition described in 12), which is an agent for preventing, treating or improving a disease against which a sigma receptor-active drug is efficacious; 16) the pharmaceutical composition described in 12), which is an agent for preventing, treating or improving a disease against which a sigma receptor antagonistic action is efficacious; 17) the pharmaceutical composition described in 12), which is an agent for preventing, treating or improving a disease against which a sigma receptor agonistic action is efficacious; 18) the pharmaceutical composition described in 12), which is an agent for preventing, treating or improving a mental disorder; 19) the pharmaceutical composition described in ~~12~~ 18), wherein the mental disorder is at least one selected from a disorder accompanied with cerebrovascular dementia and/or senile dementia, schizophrenia, emotional disorder, depression, neurosis, psychosomatic disorder and anxiety; 20) the pharmaceutical composition described in 19), wherein the disorder accompanied with cerebrovascular dementia and/or senile dementia is at least one selected from aggressive behavior, mental excitement, wandering, delirium, hallucination and hyperkinesis; 21) the pharmaceutical composition described in 12), which is an agent for improving intellectual function; 22) the pharmaceutical composition described in 12), which is an

acetylcholinesterase inhibitor; 23) the pharmaceutical composition described in 12), which is an agent for preventing, treating or improving senile dementia, cerebrovascular dementia, attention-deficit hyperactivity disorder, glaucoma, myasthenia gravis or migraine; and 24) the pharmaceutical composition described in 23), wherein the senile dementia is Alzheimer-type dementia.

Page 22

Please amend the paragraph beginning on page 22 line 3 through page 23 as follows:

In the formula (I), the "aliphatic ring" is not specifically limited, but is preferably cyclopentane ring, cyclohexane ring, cycloheptane ring, ~~or~~ cyclooctane ring~~.~~, tetrahydrofuran ring, tetrahydropyran ring, dioxane ring, dioxolane ring, piperidine ring, piperazine ring, morpholine ring or thiomorpholine ring. A preferred "aromatic ring" is, for example, furan ring, thiophene ring, pyrrole ring, imidazole ring, oxazole ring, thiazole ring, triazole ring, pyridine ring, pyrazine ring~~,~~ or pyrimidine ring~~,~~ ~~tetrahydrofuran ring, tetrahydropyran ring, dioxane ring, dioxolane ring, piperidine ring, piperazine ring, morpholine ring or thiomorpholine ring~~.

Page 23

Please amend the paragraph beginning on page 23 line 10 as follows:

In the formula (I), the repetition number m is preferably 0

or an integer of 1 to 5, more preferably 0 or an integer of 1 to 3, further preferably 0 or an integer of 1 or 2, and most preferably 0 or 1. The repetition number n is preferably ~~0 or~~ an integer of 1 to ~~3~~ 5~~, and more preferably 1 or 2~~.

Page 40

Please amend the paragraph beginning on page 40 line 14 as follows:

An assay was performed using the indanone derivatives shown in Examples 1, 13, ~~29~~ 19, 22, 27, 28, 30, ~~and~~ 33 , 37, 41, 43, 48, 51, 52, 58 and 68 below as a test compound and donepezil hydrochloride (1-benzyl-4-[(5,6-dimethoxy-1-indanon)-2-yl]methylpiperidine hydrochloride) as a control.

Page 44

Please amend the paragraph beginning on page 44 line 6 as follows:

As the test compounds, indanone derivatives according to Examples 1, 2, 7, 9, ~~and~~ 15, 37, 38, 44, 47 and 50 were used after dissolved in distilled water or ethanol. The inhibitory action of donepezil hydrochloride (1-benzyl-4-[(5,6-dimethoxy-1-indanon)-2-yl]methylpiperidine hydrochloride) as a control was determined in the same way as above.

Page 47

Please amend the paragraph beginning on page 48 line 1 as follows:

3-1) 3-(3,4-Diethoxy phenyl)propionic acid

52.3 g of 3-(3,4-dihydroxy phenyl)propionic acid was dissolved in 500 ml of ethanol, followed by addition of 5 ml of concentrated sulfuric acid. After heating under reflux for 3 hours, the mixture was left stand to cool to room temperature and evaporated. The resulting residue was extracted with a saturated aqueous solution of sodium bicarbonate and ethyl acetate. The organic layer was washed with brine, dried over magnesium sulfate ($MgSO_4$), and evaporated.

Page 53

Please amend the paragraph beginning on page 53 line 5 as follows:

5-2) Cyclo~~pentane~~heptanemethanol

1.76 g of methyl cycloheptanecarboxylate was dissolved in 20 ml of THF, followed by addition of 0.53 g of a 80% lithium aluminum hydride under ice-cooling. After stirring for 1 hour as it was, a 1 N aqueous solution of sodium hydroxide and ethyl acetate were added thereto, and solid matters were filtered off. The filtrate was dried over magnesium sulfate ($MgSO_4$), and then evaporated, to give 0.96 g (66%) of the title compound.

Page 87

Please amend the paragraph beginning on page 87 line 4 as follows:

Example 61: 1-Benzyl-4-[3-[(5,6-dimethoxy-2-fluoro-1-indanon)-2-yl]propyl]piperidine~~piperidine~~ hydrochloride